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| EXAMINER | |
|---|---|
| HUMPHREY, LOUISE WANG ZHIYING | |
| ART UNIT | PAPER NUMBER |
| 1648 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/675,444 | GIESE, MATTHIAS | |
| | Examiner | Art Unit | |
| | LOUISE HUMPHREY | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 November 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,4-12,14-19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) *21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-12,14-19,24 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This Office Action is in response to the amendment filed 20 November 2009.

Claims 2, 3, 13 and 20 have been cancelled.

Claims 1, 4-12, 14-19 and 21-25 are pending.

Claims 21-23 are drawn to a nonelected subject matter and hence are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

Claims 1, 4-12, 14-19, 24 and 25 and currently examined.

## WITHDRAWN REJECTIONS

The rejection of claims 1, 4-7, 15-18, 24 and 25 under 35 U.S.C. §102(b) as being anticipated by Chirnside *et al.* (US 5,773,235) is withdrawn in view of Applicant's argument.

The rejection of claims 9-12 under 35 U.S.C. §103(a) as being obvious over Chirnside *et al.* (US 5,773,235) in view of Krieg *et al.* (1998) is withdrawn in view of Applicant's argument.

The rejection of claim 14 under 35 U.S.C. §103(a) as being obvious over Chirnside *et al.* (US 5,773,235) in view of Gregoriadis *et al.* (1997) is withdrawn in view of Applicant's argument.

## MAINTAINED REJECTIONS

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-8, 10, 15-19, 24 and 25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Tobiasch *et al.* (2001) in view of Snijder *et al.* (1999).

The instant claims are directed to a vaccine composition, which is protective against equine arteritis virus (EAV) infections in horses and induces a cellular immune response, comprising a nucleic acid encoding a EAV sequence consisting of open reading frame (ORF) 2 of SEQ ID NO:2, ORF5 of SEQ ID NO; 5 or 9, and ORF7 of SEQ ID NO:7.

Tobiasch *et al.* teaches that EAV is a member of the Arteriviridae family that includes lactate dehydrogenase-elevating virus (LDV), porcine reproductive and respiratory syndrome virus (PRRSV), and simian hemorrhagic fever virus (SHFV). Specifially, Tobiasch *et al.* teaches prevention of EAV in horses by DNA vaccination. The cDNA sequence of ORF3, ORF4, ORF5, and ORF7 (Table 1) were molecularly cloned into the corresponding sites of expression vectors pCR3.1, pDisplay, and/or pcDNA3.1/HisC. See Abstract and on page 189-190, Molecular Cloning of Viral cDNA and Preparation of Plasmid DNA. The vaccine composition comprises one or several vectors, each comprising the aforementioned individual EAV ORF. See page 193, DNA Vaccination of Mice with Vector Construct Expressing Viral ORFs 5 and 7. The vaccine

composition further comprises PBS (p. 191, DNA Vaccination of Animals), which is a pharmaceutically acceptable carrier or excipient.

Tobiasch *et al.* does not disclose EAV ORF2, together with ORFs 5 and 7 in the same nucleic acid.

Snijder *et al.* discloses EAV ORF2, which contains the genes ORF2a, encoding a new envelope protein E, and ORF2b, encoding the small glycoprotein Gs. Both EAV E and Gs proteins are essential for the production of infectious progeny virus. Most importantly, Snijder *et al.* discloses that the minor envelope glycoprotein of 25 to 30 kDa is encoded by EAV/LDV/PRRSV ORF2 (page 6335, right column, middle sentence between the two paragraphs).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Tobiasch composition so as to combine ORF5 and ORF7 with one more antigens such as ORF2 into an immunogen expressed by the same vector. The skilled artisan would have been motivated to do so to induce a broad-range immune response against all arteriviral structural proteins, or to augment the immunogenic effect of ORF 5 and 7 with the one more structural antigen, ORF2. One skilled in the art would be motivated to generate immune responses specific for a protein structure that better mimics the wild type EAV particle complete with all structural proteins. Given the general molecular method of cloning the EAV ORFs into the same expression vector and the published ORF sequences in GenBank database as disclosed by Tobiasch *et al.*, there would be a reasonable expectation of success.

Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1,4-12, 15-19, 24 and 25 stand rejected under 35 U.S.C. §103(a)as being unpatentable over Tobiasch *et al.* (2001) in view of Snijder *et al.* (1999) and Krieg *et al.* (1998).

The instant invention is further limited to a vaccine composition comprising EAV ORF 2, 5 and 7 and further comprising a nucleic acid encoding interleukin 2 (IL-2) or further comprising one or several adjuvants.

The relevance of Tobiasch *et al.* and Snijder *et al.* is set forth above. Neither reference discloses any adjuvant in the vaccine composition.

Krieg *et al.* suggests unmethylated CpG dinucleotides as adjuvant for DNA vaccines. Specifically, Krieg et al. discloses that CpG motifs can be added deliberately to DNA or conventional protein vaccines to enhance the Thl immune response. Krieg et al. also discloses that IL-2 improves activation of antibody-dependent cellular cytoxicity. See Abstract and page 25, right column, last paragraph.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the DNA vaccine composition of Tobiasch *et al.* by adding CpG dinuleotides and/or IL-2 as taught by Krieg *et al.* The skilled artisan would have been motivated to do so to exert an essential endogenous adjuvant activity for the EAV ORF vaccines and to increase the efficacy of the EAV vaccine compositions. There would have been a reasonable expectation of success, given that CpG DNA can

directly activate both B cells and monocytic cells including macrophages and dentritic cells (See Figure 1), as taught by Krieg *et al*. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 4-10, 12, 15-19, 24 and 25 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Tobiasch *et al*. (2001) in view of Snijder *et al*. (1999) and Cantlon *et al*. (2000).

The instant invention is limited to further comprising the nucleic acid encoding equine IL-2 or a vector or expression vector comprising the IL-2-encoding nucleic acid.

The relevance of Tobiasch *et al*. and Snijder *et al*. is set forth above. Neither reference discloses IL-2 in the EAV vaccine composition.

Cantlon *et al*. discloses that in mice, co-administration of a plasmid that expressed IL-2 resulted in a significant, though modest, increase in antibody titers relative to use of the G gene vaccine alone. See abstract.

It would be obvious to one skilled in the art at the time of invention to add a nucleic acid encoding equine IL-2 or a vector containing IL-2-encoding nucleic acid to the vaccine composition of EAV ORF 2, ORF 5, and ORF 7. One would be motivated to do so because Cantlon et al. suggests that IL-2-plasmid co-administration results in an increase in immune response. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claim 1, 4-8, 10, 14-19, 24 and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Tobiasch *et al.* (2001) in view of Snijder *et al.* (1999) and Gregoriadis *et al.* (1997).

The instant invention is limited to encapsulating the nucleic acid or vector vaccine into cationic liposomes. Neither Tobiasch *et al.* nor Snijder *et al.* discloses this feature.

Gregoriadis *et al.* discloses that antigen-coding vector entrapped into cationic liposomes leads to greatly improved humoral and cell-mediated immunity. See abstract.

It would be obvious to one skilled in the art at the time of invention to modify the vaccine composition of EAV ORF 2, ORF 5, and ORF 7 by encapsulating the nucleic acid or vector vaccine into cationic liposomes. One would be motivated to do so for the purpose of improved humoral and cell-mediated immunity. Thus, the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

***Response to Arguments***

Applicant's arguments have been fully considered but are not persuasive. Applicant's response has condensed the traversal of the above four prior art rejections into one general discussion rather than directing arguments to each specific rejection. Therefore, Applicants' arguments have been addressed together as they apply to all of the four rejections under 35 U.S.C. §103.

Applicant argues that the Tobiasch article teaches away from the present invention as it discloses that the best immune response is observed in the administration of ORF5 or ORF7 alone but not when ORF5 and ORF7 are administered together. Applicant further argues that the Tobiasch article teaches away by disclosing that the results of equine arteritis virus (EAV) DNA vaccine in the mouse model do not necessarily translate to protection in a horse.

In response to Applicant's argument regarding the reduced immune response elicited by the combination of ORF5- and ORF7-expressing vectors, it is respectfully submitted that the proposed modification in the rejections at issue does not render the prior art unsatisfactory for its intended purpose or change the principle of operation of a reference. Specifically, the "30% immune response" quoted by the Applicant is the result when the neutralizing titer 1:20 is excluded, but the amount of immune response including the neutralizing titer 1:20 is actually 70% (page 195, Table 2). Consequently, the difference in the amount of immune response generated by ORF5 or ORF7 alone and by the combination of ORF5+ORF7 is not as substantial as Applicant asserted. Albeit at a lower level, the immune response elicited by the combination of ORF2+ORF5+ORF7 would be more broad and preferred by one of ordinary skill in the art because ORFs 2, 5 and 7 encode the major structural proteins of a subviral particle, which better mimics the wild type EAV particle. This rationale has already been set forth in the previous Office action mailed on 24 June 2009 on page 6 and again on page 8. Therefore, Applicant's argument is not convincing that there was a sufficient

teaching away in the art to overcome the strong case of obviousness made out by Tobiasch and Snijder.

In response to applicant's argument that the Tobiasch article does not suggest that combining ORFs from the same reading frame would offer enhanced immune protection as a matter of course, it is clarified that the reading frame was never part of the Examiner's rationale for combining ORF2, ORF5 and ORF7 into the same vector.

In response to applicant's argument that Tobiasch's disclosure does not translate to a vaccine which is protective against EAV infections in horses and induces a cellular immune response, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

In response to applicant's arguments, the recitation protective against EAV infections in horses has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan, can be reached on 571-272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin/
Primary Examiner, Art Unit 1648

14 March, 2010